

Listing of Claims

1. (Currently amended) A humanized anti-TAG-72 CC49 monoclonal antibody comprising:

a light chain comprising a light chain Complementarity Determining Region (L-CDR1), a L-CDR2, a L-CDR3, and ~~a~~-light chain framework regions 1-4 from HuCC49V10, a heavy chain comprising a heavy chain Complementarity Determining Region (H-CDR1), a H-CDR2, a H-CDR3, and ~~a~~-heavy chain framework regions 1-4 from HuCC49V10,

wherein the residues at positions 5, 19 and 21 of SEQ ID NO: 1 (light chain framework region 1) comprises ~~a~~ are replaced with threonine, alanine, and isoleucine, respectively, and the residue at position 9 of SEQ ID NO: 4 (light chain framework region 4) is replaced with isoleucine ~~e~~ corresponding framework residue from human antibody LEN at position 5, 19, 21, and 106 in the light chain,

and wherein the residue at position 20 of SEQ ID NO: 5 (heavy chain framework region 1) is replaced with valine, the residues at positions 3 and 13 of SEQ ID NO: 6 (heavy chain framework region 2) are replaced with arginine and methionine, respectively, and the residues at positions 1, 2, 4, and 15 of SEQ ID NO: 8 (heavy chain framework region 4) are replaced with arginine, valine, isoleucine, and methionine, respectively ~~e~~ comprises a corresponding framework residue from human antibody 21/28'CL at positions 20, 38, 48, 66, 67, 69, and 80 in the heavy chain;

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, as compared to ~~a~~ parental-humanized CC49 V10 the HuCC49V10 antibody, deposited as ATCC Accession No. PTA-5416.

2. (Currently amended) The monoclonal antibody of claim 1, further comprising a proline at position 9 of SEQ ID NO: 2 (light chain framework region 2) ~~e~~ corresponding human LEN framework residue at position 43 in the light chain.

3. (Currently amended) The monoclonal antibody of claim 1, further comprising a leucine at position 22 of SEQ ID NO: 3 (light chain framework region 3) ~~e~~ corresponding human LEN framework residue at position 78 in the light chain.

4. (Currently amended) The monoclonal antibody of claim 1, further comprising a glutamine at position 3 of SEQ ID NO: 4 corresponding LEN human framework residue at position 100 in the light chain.

5. (Currently amended) The monoclonal antibody of claim 1, further comprising a lysine at position 12 of SEQ ID NO: 5.

6. (Currently amended) The monoclonal antibody of claim 1, further comprising a valine at position 20 of SEQ ID NO: 5 corresponding human 21/28'CL framework residue at position 40 in the heavy chain.

7. (Currently amended) The monoclonal antibody of claim 1, wherein the light chain framework region further comprises proline at position 9 of SEQ ID NO: 2 (light chain framework region 2), leucine at position 22 of SEQ ID NO: 3 (light chain framework region 3), glutamine at position 3 of SEQ ID NO: 4, and lysine at position 12 of SEQ ID NO: 5, a corresponding human LEN framework residue at position 43, 78, and 100 in the light chain and a corresponding human 21/28'CL framework residue at position 12 in the heavy chain.

8. (Original) The monoclonal antibody of claim 1, wherein L-CDR1 comprises an amino acid sequence set forth as SEQ ID NO: 9, L-CDR2 comprises an amino acid sequence set forth as SEQ ID NO: 10, and L-CDR3 comprises an amino acid sequence set forth as SEQ ID NO: 11.

9. (Currently amended) The monoclonal antibody of claim 1, wherein H-CDR1 comprises an amino acid sequence ~~et set~~ forth as SEQ ID NO: 12, H-CDR2 comprises an amino acid sequence set forth as SEQ ID NO: 13, and H-CDR3 comprises an amino acid sequence set forth as SEQ ID NO: 14.

10 - 19. (Canceled)

20. (Original) The monoclonal antibody of claim 1, further comprising a detectable label.

21. (Original) The monoclonal antibody of claim 1, further comprising an effector molecule.
22. (Original) The monoclonal antibody of claim 20, wherein the label is a fluorescent or a radioactive molecule.
23. (Original) The monoclonal antibody of claim 21, wherein the effector molecule is a toxin.
24. (Original) A composition comprising a functional fragment of the humanized monoclonal antibody of claim 1, wherein the functional fragment specifically binds TAG-72.
25. (Original) The composition of claim 24, wherein the fragment comprises an Fv, an Fab, or an F(ab')₂.
26. (Currently amended) A humanized anti-TAG-72 CC49 comprising heavy and light chains. The composition of claim 25, wherein the antibody is encoded by a nucleic acid sequence encoding the heavy and light chains is as-deposited as ATCC Accession No. PTA-5415.
27. (Original) A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 1 in a pharmaceutically acceptable carrier.
28. (Withdrawn) A method for treating a subject with a tumor that expresses TAG-72, comprising: administering a therapeutically effective amount of the humanized antibody of claim 1 to the subject, thereby treating the tumor.
29. (Withdrawn and currently amended) The method of claim 28, wherein the humanized antibody comprises heavy and light chains and wherein is encoded by a nucleic acid sequence encoding the heavy and light chains is as-deposited as ATCC Accession No. PTA-5415.

30. (Withdrawn) A method for detecting a cell expressing TAG-72 in a subject, comprising

contacting a sample from the subject with the antibody of claim 1, and
detecting the presence of a complex of the antibody with TAG-72,
thereby detecting a cell expressing TAG-72.

31. (Withdrawn) The method of claim 30, wherein the subject has a tumor.

32. (Withdrawn) The method of claim 31, wherein the antibody is labeled.

33. (Withdrawn and currently amended) The method of claim 30, wherein the antibody comprises heavy and light chains and wherein is eneeded by a nucleic acid encoding the heavy and light chains is deposited as ATCC Accession No. PTA-5415.

34. (Withdrawn) The method of claim 30, wherein the sample is a biopsy specimen, autopsy specimen, and pathology specimens, or a biological fluid.

35. (Withdrawn) A method for *in vivo* diagnosis of cancer in a subject, comprising

(a) administering to an mammal a diagnostically effective amount of the antibody of claim 20,

(b) allowing sufficient time for the antibody to become specifically localized to at least one cancer cell, and

(c) detecting the labeled antibody *in vivo* at a site where the antibody has become localized, thereby diagnosing the cancer.

36. (Original) A kit comprising

a container comprising the humanized antibody of claim 1 and
instructions.

37. (Currently amended) A monoclonal antibody, comprising a heavy and a light chain variable region, wherein

the light chain variable region comprises a light chain framework region comprising amino acid sequences set forth as SEQ ID NOs: 41-44, and light chain complementarity determining regions comprising amino acid sequences set forth as SEQ ID NOs: 9-12;

the heavy chain variable region comprises a heavy chain framework region comprising amino acid sequences set forth as SEQ ID NOs: 49-52, and heavy chain complementarity determining regions comprising amino acid sequences set forth as SEQ ID NOs: 12-14; and

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, as compared to a parental humanized CC49-V10 the HuCC49V10 antibody, deposited as ATCC Accession No. PTA-5416.

38. (Withdrawn) An isolated nucleic acid encoding the antibody of claim 1.

39. (Withdrawn) A vector comprising a promoter operably linked to the nucleic acid of claim 38.

40. (Withdrawn) A host cell transformed with the vector of claim 39.

41. (Withdrawn) The host cell of claim 40, wherein the cell is a eukaryotic cell.

42. (Currently amended) The antibody of claim 1, further comprising a tyrosine to proline substitution in L-CDR3 at position 943 of SEQ ID NO: 11 (L-CDR3 of HuCC49V10).

43. (Currently amended) The antibody of claim 42, further comprising a valine to leucine substitution at position 27b6 of SEQ ID NO: 9 (L-CDR1 of HuCC49V10).

44. (New) The monoclonal antibody of claim 37, further comprising a detectable label.

45. (New) The monoclonal antibody of claim 37, further comprising an effector molecule.

46. (New) The monoclonal antibody of claim 44, wherein the label is a fluorescent or a radioactive molecule.

47. (New) The monoclonal antibody of claim 45, wherein the effector molecule is a toxin.

48. (New) A composition comprising a functional fragment of the humanized monoclonal antibody of claim 37, wherein the functional fragment specifically binds TAG-72.

49. (New) The composition of claim 48, wherein the fragment comprises an Fv, an Fab, or an F(ab')₂.

50. (New) A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 37 in a pharmaceutically acceptable carrier.